FAMILY PERIODIC PARALYSIS.

With a Report of Cases Hitherto Published.

By EDWARD WYLLYS TAYLOR, M.D.,

Instructor in Neuropathology, Harvard University; Assistant in Neurology, Massachusetts General Hospital; Visiting Neurologist, Long Island Hospital, Boston Harbor.

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I find no reference since Goldflam's publication in 1897 bearing directly on this subject. The series of cases above outlined, which I believe to be complete, is extremely interesting from several points of view, and especially in this connection, first, because of the fewness of all cases, and, secondly, because of the relatively frequent occurrence of the affection in certain families. Cases inadequately reported I have not, in general, included in the foregoing summary, except to allude to them under the case or cases to which the individual author pays particular attention. For example, Cousot mentions five cases, and reports one completely; Goldflam mentions twenty-two, and reports six in detail.

A critical examination of all the cases included in the list given permits us, with reasonable certainty, to exclude a certain number from the typical form of paralysis already outlined.

The early cases of Cavaré, Romberg and Gibney may rightly be questioned, chiefly on account of their association with malaria. The very slow recovery in Gibney's cases would seem to place them in a distinct, though possibly allied, category. Fischl's case is anomalous, but probably belongs to the clinical group of the periodic family paralysis. The extremely interesting family history, as reported by Rich, must also be regarded as doubtful on account of the etiology, viz., exposure, the tonic conditions of the muscles during the attacks, and the lack of information as to the reflexes and electrical conditions. Finally, Bernhardt's cases are, as he states, complicated by certain muscle changes of the dystrophic type. His patients suffered at all times from a distinct muscular weakness, although notably increased during the so-called attacks; otherwise, his cases are similar. We are justified in regarding the observations of Hartwig, Samuelsohn, Schachnowitsch, Westphal, Oppenheim, Fischl (doubtful), Cousot, Griedenberg, Pulawski, Goldflam, Burr, Hirsch, Bernhardt (with the above modification), and Taylor as the definite type of the condition under discussion. The number of cases reported by these observers is in all fifty-three. Of these, only sixteen have been described in any detail, the others occurring either in past generations, or in persons who were unavailable for a careful personal examination.

The second point is also of interest—that of the fifty-three cases, thirty-five occurred in three families, Cousot five, Goldflam nineteen, and Taylor eleven, the remaining eighteen being either sporadic, or associated with one other in the same family. From this fact alone the family character of the affection is sufficiently demonstrated.

Before entering upon a detailed analysis of this remarkable affection, it is as well to forestall a possible criticism in the use of terms by saying that in the present state of our knowledge, the word "disease" should be used with much caution as applied to this periodic paralysis. The tendency to dignify a symptom or a group of symptoms by calling it a disease entity has already been productive of much confusion of nomenclature in relation to affections of the nervous system whose pathology is obscure. As stated at the outset, the term "family periodic paralysis" is purely clinical and descriptive, and should be definitely so understood. If through a certain poverty of words we occasionally speak of the symptom-complex under consideration as a disease, it is merely as a matter of convenience, and in no way as indicative of a dogmatic belief that a periodic paralysis, as such, can in itself represent a pathological entity. Our feeling, rather, is that we are dealing here merely with a symptom, or symptoms, of extraordinary constancy, whose etiology and pathological anatomy are as yet wholly obscure. This being understood, we may profitably attempt an analysis of the condition in the light of the reported cases and of our own, leaving the most subtle problems, viz., those of etiology and pathological anatomy to the end.

The first striking feature of the condition is that it has certain constant and cardinal peculiarities. It is characterized in its typical manifestation by its heredity, by its periodicity, by its confinement to the motor portion of the nervous system, by the electrical changes, and, finally, negatively by the practically perfect health of the individual in the free intervals. We shall consider each of these cardinal symptoms in detail.

Heredity: The affection is distinctly of a family type. In Cousot's cases five members of one family were affected; in Goldflam's nineteen, and in ours eleven. Schachnowitsch and Hirsch each report two cases as occurring in parent and child, and Goldflam again three in one generation. The other few cases are sporadic. In the condition described by Rich, twenty-two members of the family were affected, of whom fourteen were still living when his paper appeared. The two family histories of statistical interest are those described by Goldflam and Taylor. In Goldflam's family the predisposition was transmitted on the mother's side, through both male and female lines. It was not associated with other neuroses of any sort. Many of the family were entirely free. In my cases, also, the affection is on the mother's side, beginning with a male five generations back; from him transmitted to a son, thence to two daughters, one of whom had six children, three sons and one daughter, all but two being affected. Several of this generation are now living, but I have been unable to secure any definite data. The other daughter of the previous generation had three children, one of whom, the mother of our patients, was affected. She, again, had three children, two of whom, a son and daughter (our patients), are sufferers from the condition, the other son having no trace of it whatever. It is, therefore, seen that in our cases the transmission has been absolutely direct through two females and two males. Those who have been exempt from the condition themselves have in no case transmitted it to their children. (Vide chart.) As regards other possible hereditary taint in the family, we find none of significance. One member in the second generation had epileptiform convulsions, but was not afflicted with periodic paralysis. The mother of our patients died of tuberculosis, and, possibly, their grandmother. To this fact we can attach no importance, as already stated. No other significant heredity appears.

In general it may be said that these cases have occurred in families of unusual nervous stability (See abstracts of histories); in no case do we find any evidence whatever of a degenerative family history. If a neurosis at all, it is distinctly not one of a degenerative type. The mental superiority of our family and its freedom from other nervous derangement is noteworthy.

Periodicity: A characteristic of the condition is its recurrence. The alternation of attacks of loss of motor power, with intervals of perfect health, is the peculiar feature which lends to the affection one of its chief interests. This periodicity is governed by no discoverable law, and varies greatly in different cases. From a condition of health, so far as the patient knows, he is more or less suddenly plunged into a state of helplessness, which, again, lasts a varying time, to give place in turn to a period of normal activity. Details of individual cases are not here necessary, inasmuch as the fact of periodicity applies to all, and is to be regarded as a fundamental characteristic.

Motor Paralysis: Another equally important and fundamental peculiarity is the absolute confinement of the affection to the motor sphere. Apart from certain doubtful subjective sensory disturbances, there is no evidence whatever to show that the sensory side of the nervous system is ever involved in the process. In our most carefully studied case there is no indication during the attack of the slightest sensory involvement. Tests for various sorts of disturbed sensation were wholly negative in result, nor was there ever any subjective complaint of pain or paræsthesia. It was noted at the examination made during an attack that strong faradic currents were borne without complaint, but this, we believe, was due rather to the failure of muscles to respond adequately than to an actual blunting of the feeling. This is so common in observation that further comment is unnecessary. It was furthermore observed that between the attacks there was small complaint of pain from strong currents. He is, perhaps, unusually tolerant of the peculiar sensations produced by electricity, as one frequently sees in non-neurotic persons.

In Case II., the sister, there is also no sensory disturbance, beyond a dull pain, following a severe attack, in the muscles affected. J. also complains at times of a feeling of soreness, which is evidently due to a natural local disturbance in the muscles themselves, following the paralytic stage.

The following vague disturbances of sensation have been described by previous observers: Hartwig speaks of a sense of numbness and formication in the paralyzed part, while finding objective sensibility unaffected. In Schachnowitsch's second case there were subjective sensory disturbances as precursors of the actual attack. In the Westphal-Oppenheim case there was an antecedent prickling sensation in the legs, and Oppenheim also noted a sense of prickling in the soles of the feet in the course of an attack, with otherwise perfectly normal sensibility.

Fischl, on the other hand, found in his case a distinct blunting of sensation in the affected areas, with, at times, an ice-cold surface temperature. This fact, in conjunction with the generally anomalous course of the case, a certain mental involvement, with lack of heredity, would seem to render it doubtful of classification, and we have so regarded it. Goldflam alludes to an annoying itching, chiefly between attacks, and also just previous to recovery from an attack. In Hirsch's case there were occasional sharp pains in one foot. In no case, excepting that of Fischl, was any objective change found, and the foregoing slight subjective disturbances we must regard as inconstant and unimportant.

The mind has in all cases remained unaffected, whether during or between the attacks. An occasional drowsiness has been observed, which in Fischl's anomalous case came to be practically an equivalent of the typical attack. The disturbance of the nervous system in these cases may, therefore, be regarded as essentially motor in its manifestation. This is a constant symptom. The distribution of the paralysis, however, varies in different cases, and at different times in the same patient. This will be considered in detail later. The paralysis is in all cases flaccid in type.

Electrical Changes: In general it may be said that there is a loss of direct and indirect electrical excitability, varying from absolute loss to both currents, to slight quantitative diminution, depending upon the completeness of the paralysis. Between the attacks the conditions have usually been normal or only very slightly abnormal. Exhaustive examinations have been made into the electrical peculiarities, chiefly by Oppenheim and Goldflam. Oppenheim found that at the height of the attack there was complete loss of reaction in certain groups of muscles, with an increased skin resistance. The return of reaction to faradism and galvanism was gradual, like the return of motor power. There was always quantitative diminution during attacks. Response, when obtainable at all, was quick. No R. D. The results of Oppenheim's electrical examinations were not entirely uniform. Later observations on the same patient showed a slight atrophy of those muscles which had the poorest reactions between the attacks.

Goldflam also has examined his cases with extreme thoroughness, and with interesting results. In addition to the quantitative changes, up to complete loss, observed during attacks, Goldflam describes certain changes in the free intervals, which he regards as of the utmost significance and importance. In two of his cases, brothers, he found the direct and indirect irritability markedly diminished to both currents between the attacks, associated with rapid fatigue. The character of the contraction was also changed; it was slow, and there were, in addition, various polar changes. Partial R. D. was obtained and both Ca. C. Te. and An. C. Te. with weak currents. He found qualitative changes more prominent in the free intervals, and quantitative, often up to complete loss, in the actual attacks. Other observers have all noted the quantitative diminution of electrical excitability during the attacks, but have in general found the condition between normal in this, as in other respects. With the possible exception of Oppenheim, however, no one has so thoroughly investigated the matter as Goldflam. In our own case a quantitative diminution to faradism, which it was alone possible to use, during the attack was pronounced. Noteworthy in our case was a quantitative diminution in the facial nerve and its distribution. Between the attacks we could demonstrate absolutely no polar changes whatever. Response was also quick and normal to faradic and galvanic currents. There was an apparently increased skin resistance, alluded to by Oppenheim as occurring during the attacks. The only noteworthy peculiarity in our case was the failure of reaction of the right peroneal group of muscles. In the light of

Goldflam's researches, this fact may be of more significance than we are at present disposed to grant. Future examination will demonstrate its importance, if it have any. Considering the fact that all other muscles and nerves tested responded normally, we would reserve judgment of the unexplained failure of this one group.

The general changes regarding the electrical changes may be summed up by saying that there is a loss or marked quantitative diminution during attacks, and considerable evidence of a disturbed neuromuscular excitability in the free intervals, not yet demonstrated as constant.

Reflexes: Hardly less noteworthy than the electrical changes is the behavior of the reflexes. In all cases, when any mention is made of the matter, the deep reflexes, of which the knee-jerk is the type, have been reported lost during the height of the attack, and present in the intervals. This was verified in my case. The same holds true, in general, of the peripheral reflexes, though not to the same degree. Oppenheim reports: Plantar, lacking; cremaster and abdominal, present; Hirsch: Peripheral reflexes lost, excepting abdominal, which were weak; Taylor: No plantar; cremaster, slight; abdominal and epigastric, active. Pulawski and Goldflam, on the other hand, report cutaneous reflexes present. The disturbance of the reflexes depends apparently wholly upon the extent of the paralysis. Inasmuch as the legs are most often and most completely involved, we find an explanation of the constant loss of knee-jerks, and the greater frequency of the loss of the plantar than the other cutaneous reflexes. With our relative lack of knowledge of the peripheral reflexes, nothing further is to be said. Our chief interest centres in the knee-jerk.

The Free Intervals: We have maintained that the patients suffering from this affection are normal between the attacks. This is, in general, true, but the rigid examinations to which certain of the cases have been subjected would seem to throw doubt upon its absolute acceptance. In our cases nothing abnormal was found; the patients themselves feel and, so far as they know, are perfectly well and strong, excepting at the time of the attack. This has been the usual verdict. Oppenheim, however, found slight atrophy of the hand muscles in his case, and later weakness of the legs, associated with constant defect in electrical reaction. Goldflam describes in detail electrical abnormalities between the attacks, and definite changes in the muscular system, upon which he bases his theory of the affection. Bernhardt, whose cases we have considered somewhat atypical, found muscle changes, which he regards as allied to the dystrophies, from the beginning of the affection or even before. With these exceptions, the general statement stands.

In the foregoing discussion we have pointed out what may be looked upon as the cardinal symptoms of the family periodic paralysis. These symptoms are so constant that their absence would rightly throw doubt upon the diagnosis. They are: Periodicity, flaccid motor paralysis, loss of electrical excitability, loss of deep reflexes, and, between attacks, relatively perfect health.

Other symptoms vary somewhat in different cases, and for this reason demand a painstaking analysis. We shall attempt to describe them in as systematic a manner as possible, omitting for the time being any discussion of possible causes.

Attack; Prodromata: Various symptoms have been described as occurring immediately antecedent to an attack, though none of them are constant in all cases. Hartwig's patient had a feeling of weariness, with some sweating and considerable numbness and formication. Westphal-Oppenheim noted heat and sweating, with a desire to urinate, which could not at once be satisfied. Fischl's (doubtful) patient had headache, backache, poor appetite, somnolence, rapid pulse, with a normal surface temperature of the head, body and arms, and an icy-cold temperature of the legs, associated with great pallor, suggesting a vasomotor disturbance of a violent sort. Cousot found feebleness of articulation and a desire to walk. Goldflam, in his best observed case, alludes to the fact that the attacks usually came on Friday, no doubt a coincidence; that the patient had itchings on the well evenings, but none on the evenings preceding the attack; that he was capricious as to food, and was later annoyed by a feeling of coldness in the legs and by occasional thirst. In my best observed case there are no prodomata whatever, excepting a feeling of weakness, which is rather a part of the actual attack than a warning of its onset.

Evidently, then, these prodromal symptoms are exceedingly inconstant. Sweating and thirst are most frequent, but they are much more often absent than present. The fact that the attacks come on so frequently at night may explain the fewness of the prodromal symptoms.

Age of Onset: The age at which the attacks usually begin varies within somewhat narrow limits. The data on this point, so far as obtainable, are as follows: Cavaré, before twenty-one; Hartwig, at twenty-three; Samuelsohn, at eighteen; Westphal, at twelve; Fischl, at eight; Cousot, four cases at fourteen, nine, ten and ten, respectively; Griedenberg, before twenty-one; Pulawski before twenty-one; Goldflam, case chiefly studied, at thirteen. The mother of Goldflam's case had but one attack, at thirty-six. Goldflam also refers to a number of young children similarly affected, who are said to have died during attacks. Burr's case began at ten, Hirschs at the nineteenth or twentieth year, and Taylor's first case at fourteen or fifteen; the second at twelve. Of the other nine cases in the family, the tradition is that the attacks began always at or about the time of puberty. The latest case was at eighteen.

From these statistics, it will appear that the affection is evidently one that owes its origin to certain conditions prevailing in youth and the developmental period of life. With the exception of a few cases mentioned by Goldflam, the onset has always been before the twenty-fourth year, and, in the great majority of best reported cases, it has been between the tenth and twentieth years of life. Of those reported under the tenth year, Fischl's is very doubtful, as before stated. Cousot's was imperfectly reported, as also Goldflam's cases occurring in childhood.

Sex: In general there seems to be no discrimination as to sex, though it happens that in the carefully reported cases there are but three females—reported by Fischl, Goldflam and Taylor. The affection is transmitted, however, equally through the female line. Of the eleven cases in Taylor's family, five were women.

Muscles Involved: The most constant feature in this regard is the paralysis of the lower extremities. In the typical cases the legs are always affected, usually first and most severely. Body and arms are later involved in the severe attacks, as are also the neck muscles. Very unusual is an involvement of any of the cranial nerves. An analysis of the observed cases shows certain variations from the general rule. Burr, for example, found in his case a hemiparesis, not, however, involving the cranial nerves; ordinarily, the paralysis was bilateral. Hirsch, in one attack of his patient, speaks of the weakness beginning in the arms. In Romberg's case and Fischl's cases the attacks were practically limited to the legs, as they were at times in Griedenberg's case. Cousot noted feebleness of articulation as an early symptom, with difficulty later both in speech and deglutition. The usual description, however, is: Legs, arms, body, head involved; cranial nerves free, coughing and sneezing often impossible; at times superficial respiration. With slight variations these were the conditions found by Hartwig, Samuelsohn, Westphal-Oppenheim, Pulawski, Goldflam, Hirsch and Bernhardt. In our own case the paralysis is unusually complete. Legs, body, arms, neck muscles are always involved in these severe attacks. Most noteworthy, however, is the observation that the facial nerves are occasionally included, to a less degree, and in the case of Mrs. G. (Case II.) the motor branches of the trigeminal nerves are slightly affected in the most serious attacks. In her case, also, a threatening dyspnœa, alluded to also in Goldflam's second case, has occurred in her worst attacks.

The distribution of the paralysis is sufficiently constant to justify the general statement that its greatest severity is in the leg muscles, and that it gradually grows less the higher on the body we go, the ocular nerves, for example, never being involved, and, so far as we know, the fifth only in our one case. The involuntary muscles are not affected.

Order of Involvement of Muscles in Attack: We have already, in a preceding paragraph, indicated that the legs are first affected, and later the other portions of the body in a somewhat regular sequence. The exact determination of this point in our case and in others is difficult, owing to the fact that the paralysis usually comes on during sleep, and the patient finds himself on waking completely paralyzed. My patient J., for example, could give me no definite information as to which muscles were first affected. His general impression, however, is that the legs first grow weak.

Mechanical Irritability of Muscle and Nerve: Goldflam lays stress upon the fact that the mechanical nerve-muscle irritability is markedly changed during an attack. Irritability of the muscles through tapping or pressing a nerve, in his case, was often totally lost. The idiomuscular irritability was altered in such a way that the fascicular contractions in the muscles were lost, and later the transverse swellings occasioned by the blow also disappeared. The return of the mechanical irritability of the muscles and nerves he found antedated somewhat the return of electrical excitability. Goldflam regards this observation as of great importance, though, naturally, secondary to the still more remarkable electrical changes. Hirsch speaks of the idiomuscular irritability being less than the normal in his case.

Order of Recovery: It appears from a study of the cases that the order of return of power is the inverse of the onset. As a rule, recovery begins in the upper extremities, and extends later to the legs.

Rapidity of Onset and Recovery: The usual rule is, so far as it is possible to observe, a gradual onset, usually of several hours, at times of several days, before the height of the paralysis is reached; a stationary stage of varying length, and an equally gradual recovery in the order named. A sudden loss of power and a sudden recovery are exceedingly rare. Hirsch reports a sudden recovery, and also Fischl, from one attack, and Goldflam a sudden onset.

Time of Onset: It is usually at night. Schachnowitsch, Westphal-Oppenheim, Cousot, Pulawski, Bernhardt and Taylor report cases in which the patient wakes paralyzed. This is always so in my best reported case. The other case, Mrs. G., has attacks not infrequently which begin during the day.

Length of Attack: This varies within very wide limits, from less than an hour (Fischl) to a week (Burr). The usual duration of a well-pronounced attack is from ten to forty-eight hours. The length varies greatly in the same patient at different times. It is a common experience for my patient J. to be unable to leave his bed before 11 or 12 o'clock, and hardly less common for him to be helpless until evening. (Vide letter). He also has frequent feelings of weakness, which may hardly be called actual attacks. These feelings are rather precursors of the most serious ones, which are sure to come. In general, the longer the attack, the more complete the helplessness and the more profound the reflex and electrical changes.

Frequency of Attacks: Nothing definite is to be said on this point. Goldflam speaks of a case in which but one attack occurred during life, and that in the thirty-sixth year. In one of my cases the attacks occur at times daily, and frequently several times weekly, with intermissions. Cavaré and Romberg spoke of a quotidian type, which they associated with malaria. Samuelsohn's case had two attacks a year for a while; Hirsch's, one yearly for a certain period; Westphal's, one every four and six weeks; Goldflam's, weekly to yearly. There is in this absolutely no constancy. It is to be observed, however, that each invidual has a certain type of attack, which may vary greatly in degree, but not markedly in kind. Since the onset of the affection in my case J., scarcely a week has passed without some intimation of its presence. His sister, on the other hand, is entirely free for months at a time.

Total Length of the Affection: Although, for obvious reasons, definite information is somewhat uncertain on this point, yet the stated or implied belief of the various writers on the subject is that the attacks continue unchanged and unchecked through life. There is no intimation that they grow less or cease. Of very particular interest, then, is the statement made in regard to my family, that in all the cases the attacks have tended to grow less with advancing years, and finally to disappear entirely between forty and fifty. There are at present members of the second generation living who have had, but are now practically free from the attacks. In view of Goldflam's and Bernhardt's theories, later to be discussed, this fact must be of great importance.

Abortive Attacks: There is no adequate evidence to show that an attack is ever actually aborted. Schachnowitsch, Goldflam and Taylor found that active muscular exercise had the effect of postponing an attack. This is very striking in my case. A feeling of weakness may be dispelled by walking, for example, but he is sure that it is merely temporary, and that he pays all the more dearly, perhaps the next day, for his temporary escape. A relapse before recovery has entirely taken place may occur, as shown in my case, described in detail under his personal history. This is unusual.

Equivalents: The only instance we have been able to find of what may properly be called an equivalent is that described by Fischl. In place of the paralytic attack, his patient, a child of eight, developed a peculiar drowsiness, which came on in paroxysms, from which he finally fully recovered. The case is in general too uncertain to render the observation, in this connection, of value.

Heart: Oppenheim was the first to call attention to a remarkable temporary affection of the heart. His observations were later verified by Hirsch. Oppenheim found a slight but definite enlargement, with murmurs indicative of mitral insufficiency, during the attack, which quickly gave place to normal conditions when the paralysis disappeared. Goldflam describes the heart as arythmic in action at times, with a weak, blowing systolic murmur at the base and a slight accentuation of the second sound, combined with a slow pulse, and no other evidence of circulatory disturbance. This condition, however, excepting the arythmia, persisted in the free intervals; there was no enlargement of the heart, and, in general, the disturbance could not be attributed to the direct influence of the attack, unlike Oppenheim's case. In view of a later case, Goldflam has somewhat modified his view. Hirsch found almost precisely the same condition that Oppenheim had—area of dullness enlarged, first sound at apex impure, slight accentuation of the second pulmonic, insufficiency of the mitral valve; pulse regular, 78. The morning following the attack, the heart was practically normal. Up to this time I have not been able to find any temporary heart abnormality in my case. To determine the point positively, however, repeated examinations in a large number of attacks should be made.

The pulse shows no noteworthy change during the attacks, and, in general, it may be said that, apart from a temporary heart dilatation noted in two cases, not much is to be learned from a study of the circulatory apparatus.

Temperature: Nothing noteworthy. Changes in superficial temperature were observed in Fischl's doubtful case.

Bladder and Rectal Functions: It is an interesting observation that in my case the desire to pass urine or fæces is abolished during the attack, even if of thirty-six hours' duration. This is never due to a true retention, but to a lack of desire. The patient himself explains it on the ground of his helplessness, and the consequent discomforts of either act. This evidently is hardly a sufficient explanation. Probably somewhat less urine is secreted than under normal conditions, and certainly much less water and food are ingested. (See previous remarks on appetite and thirst.) This, with the general atony of the muscles, no doubt brings about the condition; it is not incapacity, but, rather, lack of necessity. Westphal speaks of a desire to urinate as a preliminary symptom, with a temporary inability to do so. With this trifling exception, we find no mention of disturbance of the rectal and bladder functions. When the matter is mentioned at all, the writers speak of the condition as normal and the sphincters as uninvolved.

Other symptoms alluded to in the reported cases are too infrequent and inconstant to require individual consideration.

It will be impossible and undesirable to draw a sharp line between the pathological anatomy and the etiology of this affection. For the sake of clearness of exposition, however, we shall attempt to consider these two final matters under separate headings.

Pathological Anatomy: There are no constant changes in any of the internal organs; the only temporary change as yet described is a dilatation of the heart during an attack (Oppenheim, Hirsch). The spleen has shown no alteration between or during attacks. Inasmuch as death from this cause is practically unknown, no minute postmortem examination of the nervous system has been made. Nor can we suppose any constant lesion of the nervous mechanism, demonstrable by the microscope, could, under most favorable conditions, be found, since intervals of health, certainly so far as the nerve mechanism is concerned, alternate with the typical attacks. Leaving aside for the moment the etiology, it is evident that the chief interest of the affection, from the point of view of pathological anatomy, must centre in the muscular system, although certainly no adequate explanation of the origin or nature of the attacks is to be sought in the muscles themselves. Excision of a small bit of muscle has been practiced both by Oppenheim and Goldflam, who have arrived at quite contrary opinions as to the significance of their findings. Oppenheim describes a bit of muscle, excised from the deltoid, as showing a waxy degeneration, which he regards, however, of most doubtful pathological significance. He attaches, in fact, no weight whatever to the observation. Goldflam, on the other hand, from a study of muscles from several of his cases, using muscle from a cadaver as control, comes to the conclusion that the pathological changes in the muscle are of extreme importance, and offer at least a partial explanation of the clinical picture. He found an increased diameter of the individual muscle fibres, a general hypertrophy of the fibres, a rarefaction of the primitive fabrillæ and vacuole formation. To these muscle changes Goldflam attributes the persistent electrical anomalies, which he alone has found constant between the attacks. Such changes, or any permanent changes whatever, manifestly do not explain the periodic paralysis. Oppenheim's and Siemerling's[9] investigations would indicate that in so far as Goldflam drew conclusions by comparison with muscle from the cadaver he was in error. This point Goldflam, in general, admits, but feels none the less confident that definite pathological changes were present. In his last article Goldflam reiterates the ideas previously expressed.

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[9] Oppenheim-Siemerling: Centralbl. f. med. Wissenschaften, 1889, pp. 705, 737.

Beyond this we have no knowledge as to the condition of the muscles. Bernhardt's cases are interesting in this connection, inasmuch as his patients from their earliest years had constant difficulty in the use of certain muscles, entirely apart from the periodic attacks. For this reason, because of the almost undoubted muscle changes in Bernhardt's cases, as he supposed of an allied sort to the various dystrophies, we have hesitated to include them among the uncomplicated forms of so-called family periodic paralysis. The justification for this may seem doubtful in the light of Goldflam's researches, but we have been led to this standpoint for the reason that in our family recovery from the attacks always occurs at about the fiftieth year. If a dystrophy, which both Goldflam and Bernhardt supposed, were at the bottom of the difficulty, it is not easy to explain this fact, which appears absolutely undoubted in our family. As before stated, the changes described by Goldflam may be an accompaniment but can in no way be regarded as causative of the periodic attacks, which, after all, constitute the so-called disease. It will be remembered, also, that Oppenheim found a slight muscular atrophy in the hand muscles, but apparently does not take the position that the affection is to be classed with the muscular atrophies or dystrophies, Goldflam does not hesitate, however, to say that through his researches on the muscle he has placed the affection in the category of the organic diseases. His own words are: "Durch diesen Muskelbefund ist die paroxysmale Lähmung aus der Reihe der Neurosen geschieden, sie tritt in das immer sich erweiternde Gebiet der auf organischen Störungen beruhenden Erkrankungen, speciell muss sie in die grosse Kategorie der bereits bekannten familiären (mit gleichartiger Vererbung) Erkrankungen eingereiht werden, als welche die Dystrophia muscularis progressiva, die neurotische Muskelatrophie Hoffman's, die Friedreichsche Krankheit, die Myotonia congenita zu nennen sind."[10]

Bernhardt is inclined to the same opinion; others would, as yet, not be so dogmatic.

As to the location of the process, whatever it may be, which produces the paralytic attacks, we may certainly limit it to the spinal motor neuron and its associated muscles. Westphal suggested, as an explanation, a periodic disturbance of circulation in the cord. Were such a circulatory disturbance the cause, we should have to suppose a limitation of its action to the anterior horns, since sensation is not affected. This is evidently a mere assumption, and also, in the light of later researches, does not explain the observed facts. Oppenheim has suggested a similar circulatory disorder in the periphery, which certainly may exist, but is difficult to prove. What evidence we have goes to show that the periodic disturbance is peripheral, and probably associated with the terminal distributions of the nerves in the muscles, and almost undoubtedly with the muscles themselves, as shown by the loss of myotatic, as well as nerve, irritability. Were it necessary to find a single point of disturbance, we should locate it in the muscle rather than in the nerve or its endings. It is, however, altogether possible, and incapable of refutation, that it may be the result of a temporary lesion in both muscle and nerve.

The *blood* shows certain changes of interest in the few cases in which it has been examined. In my case Dr. H. F. Hewes has twice studied the blood, both specimens being taken during the free interval.[11] The details of his reports have already been given under the clinical history. In general, he found a lymphocytosis, with no evidence of anæmia; a large percentage of basophiles, which he regards as characteristic of a reduced condition of nutrition. The count, he states, would be normal for a child of ten, but not for a man of twenty. Dr. Hewes finds also a relatively small number of white corpuscles.

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[10] Goldflam: Loc. cit. Ref. 18, p. 27.

[11] Unfortunately it has, as yet, been impossible to make an examination of the blood and urine taken during the attack.

Goldflam alone of the other observers reports a blood examination. Klein, who made the examination found a constant but varying leucocytosis during the attack, which was normal in the intervals. Noteworthy is the fact that Klein also found a definite lymphocytosis, 40 per cent., in the free intervals, which is identical with Hewes' observation. In the free interval eosinophiles often show an increase to 5 per cent. In the attack there was a marked neutrophile leucocytosis, with a reduction in the number of eosinophiles. The blood, therefore, in both Goldflam's case and mine shows distinct pathological qualities. We may not, however, draw deductions from this fact; it is quite impossible for us to say in what relation the blood changes stand to the paralytic attacks. It is, however, probable that both are due to a common cause, of which we have as yet absolutely no definite knowledge.

The ordinary routine examination of the *urine* in the various cases has shown nothing, excepting in Goldflam's later cases, in which traces of albumin and pathological cells were found during an attack. Goldflam again was the first to make a detailed study in order to determine, if possible, the presence of a toxic substance, to which might be attributed the periodic attacks. His efforts were, in part, successful. The analysis was made by Knaster, and resulted in the isolation of certain substances whose toxic effect, however, could not be demonstrated on animals. A rabbit, for example, injected with the supposed ptomaine, died, but with none of the symptoms of the periodic paralysis, as seen in man. The injection of the urine itself seemed more toxic when the urine was taken during an attack than in the interval. These investigations must be regarded as, in general, negative, and certainly show nothing as to the pathology of the affection. The examination of a twenty-four-hour specimen of urine in the free interval in my case suggested a somewhat low condition of metabolism. The excretion of urea was below normal for a person of his age. The twenty-four-hour amount was also low. Otherwise, the urine was essentially normal. (Details are given under clinical history.)

Examination of the stools has thrown no light on the question. It has not been made in my case, and there is no evidence that it has been done by any observer with anything approaching adequate thoroughness.

Etiology: The exciting cause of these periodic attacks has been up to this time absolutely elusive, and no doubt will remain so until our methods of investigation are much more highly perfected than now, and until we are able to distinguish clearly causes from effects, and concomitant conditions from both. There is evidently a striking hereditary predisposition in the affection, which, naturally, in no way helps to explain the exciting cause. The association of the attacks with malaria led several of the earlier writers (Hartwig, Cavaré, Gibney) to bring the two conditions into casual relationship. Apart from the doubt which attaches to the classification of certain of the cases, notably Gibney's, it would appear that the mere fact of periodicity possibly led to the idea of malaria as a cause, an error from which we are not yet wholly free. Now that we are able to demonstrate the malarial organism, there is no possibility of the perpetuation of this error. The organism has never been found in cases of periodic paralysis, and as our clinical knowledge has grown, it has become more and more evident that the condition has no affinity to malaria beyond the superficial fact of its periodicity.

An observation which we have made in common with others is that the attacks almost invariably occur at night, and, what is more important in this connection, that they are usually preceded by a day of exceptional muscular activity. My patient is able, with a certain degree of assurance, to predict an attack from his previous day's employment. A long bicycle ride on a tandem, in which he was obliged to do most of the work, led to one of the worst attacks the following night and day he has ever had. Such experiences are common with him, though not absolutely invariable. Not less interesting is the fact that the attacks never come on while he is exercising, a common observation of others as well, but only after he has rested and, preferably, slept. Our conclusions from these relatively constant facts must simply be that muscular exertion, followed by muscular rest, is the condition of an attack.

This statement of the fact, however, brings us no nearer the actual exciting cause. Bernhardt, Oppenheim, and especially Goldflam have urged the probability of an autointoxication of some kind, the conditions of whose activity are given by exercise, followed by rest. Van Gieson[12] in his recent paper expresses a like opinion, and certainly, to us, no other cause seems adequate. In this case we must suppose that, depending upon a family peculiarity in certain stages of metabolism a poison is generated within the system, whose action is paralyzant to peripheral motor nerves and muscles. The analogy to curare has been suggested by Bernhardt. It is interesting, but not altogether apt, inasmuch as the effect of curare is confined to the nerve, whereas in the periodic paralysis the toxic agent, whatever it may be, leads to a loss of myotatic irritability as well. Further speculation on this point is unprofitable. We, as yet, have no demonstrative evidence of the theory of autointoxication. Nevertheless, it remains by all means the most plausible working hypothesis. The source of origin of the problematic poison is wholly obscure. In the hope of finding some light, careful investigation as to the digestive functions has been made, with no result. It is quite impossible in my case or others to logically trace an attack to a dietary error, or to a possible retention in the body of fæcal matter. The lack of appetite during attacks cannot be looked upon as of the slightest significance in this connection.

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[12] Van Gieson: The Toxic Basis of Neural Diseases, State Hospitals Bulletin, 1896, I., No. 4, p. 470.

For obvious reasons syphilis, neuritis and hysteria play no part in the etiology. Emotions have, in certain cases, seemed to have some effect in the production or checking of an attack, but not to a significant extent.

The results of pathological and etiological investigations hitherto made are, therefore, positive as regards actual muscular changes (Goldflam, Bernhardt) in certain cases, and entirely negative as regards the nature of the substance, if such it be, which causes the periodic attack. The pathological changes in muscle and, possibly, in blood and urine are interesting,as facts, but not as explanation.

Diagnosis and Classification: The affection presents no difficulty in diagnosis when occurring in a typical form. The combination of symptoms is unique and unmistakable. Goldflam has in one case of Landry's paralysis temporarily made a diagnosis of paroxysmal paralysis.

The classification of the disturbance offers much greater difficulty. As already indicated, Goldflam and Bernhardt are strong in their belief that the affection should be classed among the dystrophies as an organic disease of the nervous system, giving as an argument that changes (Goldflam) are found in the muscles. Admitting this fact, however, the periodic paralytic attacks, which alone are significant, remain totally unexplained, inasmuch as most dystrophies occur without such attacks. Goldflam admits to a certain extent the inconsistency, but retains his somewhat dogmatic position. In our opinion, and particularly in our family, we feel altogether justified in subordinating any possible muscular changes, and fixing our attention solely on the attacks, which are the disease, as clinically observed.

To our mind, a more interesting and instructive analogy is that between this affection and the so-called congenital myotonias. Although differing widely in manifestation, the two affections at least have this in common, that they occur paroxysmally.

In this connection a reference to Rich's cases is of interest. It will be remembered that in his cases cold was invariably the exciting cause of the attack, but that the attack was always of the character of a tonic spasm. In this curious family history we no doubt have to do with what Eulenburg has described as Paramyotonia Congenita, a disturbance allied to myotonia of the ordinary type. Further study of these spasmodic affections of the neuromuscular system in relation to the flaccid periodic paralysis will no doubt yield much of interest. To ally the conditions under consideration with the muscular dystrophies is surely a begging of the real question at issue. Goldflam, however, states that the periodic paralysis has the closest analogy with congenital myotonia, but our knowledge of the pathology of myotonia is evidently too vague to admit of dogmatic statement. That periodic paralysis is to be included in the general etiology of the hereditary affections goes almost without saying, but we are overstepping our knowledge when we attempt too closely to force its relationship to any one.

Prognosis: It is usually good so far as life is concerned. Apart from young children, but two deaths have been reported, one of doubtful significance, the other apparently induced by a therapeutic attempt. My family has the peculiarity of showing a tendency to recover in middle life. Others reported have remained unchanged through life, so far as observed.

Treatment: Absolutely unavailing. It is evident that a successful treatment is not likely to be instituted until a cause is found; drugs, including quinine, in the undoubted cases have been entirely inefficient.

The affection discussed in the foregoing pages evidently offers one of the most subtle problems with which medicine has to deal. The clinical phenomena are extraordinarily well defined; the pathological anatomy is vague; the etiology is absolutely obscure. The solution of the problem already reaches far beyond the field ordinarily occupied by the neurologist; a laborious investigation into the chemistry of the metabolism of so peculiarly predisposed a series of individuals may finally bring the desired solution. At present, excepting that the problem is more definitely stated, we are not further advanced than was Westphal, more than ten years ago, when he said: "Wir stehen somit dem geschilderten Krankheitsfalle als einem Räthsel gegenüber."

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DISCUSSION.

Dr. Wharton Sinkler, in connection with the paper of Dr. Taylor, wished to place on record a case which came under his observation last summer. The patient was a man with facial paralysis, who gave a history of five previous attacks in the course of about ten years. Each of these lasted several weeks, and ended in complete recovery. No satisfactory cause for the attacks could be elicited.

Dr. C. L. Dana had seen a number of cases of periodic paralysis; none, however, of the family type. From his observation of these cases, including the one reported by Dr. Gibney, he had come to the conclusion that, while some of them were cases of recurrent poliomyelitis, the majority were purely hysterical in character. The speaker expressed the opinion that the question of periodical paralysis due to malaria was still unsettled. He had never seen any cases of that kind, and in several instances where patients were sent to him with that diagnosis, the paralysis proved to be simply functional or hysterical.

The family type of the disorder reported by Dr. Taylor was extremely interesting. It was certainly rare, and, perhaps, a little light might be thrown upon the subject by studying allied conditions. Dr. Dana said he had seen a number of patients who had informed him that when first waking in the morning they were unable to move for half an hour, or even longer. They suffered from waking palsy and a certain amount of waking numbness. Cases of ptosis are not uncommon, and the same is true of cases of morning sweating, where the patients become bathed in profuse perspiration just as they awaken. Other peculiar morning disorders are known, and perhaps these palsies may be in the same category. Dr. Dana said he had always regarded them as the result of diathetic disturbances. They usually occur in persons of the neurasthenic or lithæmic type, and in the former they are probably associated with a congenital disturbance or defect of the nervous system. The ordinary types of morning paralysis seem to be the result of some toxic condition, associated with an asthenic condition of the nervous system.

Dr. Joseph Collins had observed three cases of periodic paralysis; none, however, of the family type. One of the cases had been reported by him under the title of asthenic bulbar paralysis, and it was a typical example of that affection. When Dr. Collins first saw her, her symptoms were those of profound neurasthenia. About two years after the commencement of her illness she had double ptosis, double facial paralysis, paralysis of the extremities, more marked in the upper, and ballooning of the abdomen; her general condition being very similar to that of surgical shock, and indicating an overwhelming disorder of the sympathetic nervous system. After a few days' duration the paralytic manifestations disappeared. Sensory disturbances were never noted. In the course of two or three years she had had about five attacks similar to this one, and in the interval the symptoms of asthenic bulbar paralysis persisted.

The second case was a woman who had been referred to him by Dr. Fordyce. She had complete motor and sensory paralysis on one side, and the hand and forearm, as well as the foot, of the same side showed the manifestations of Raynaud's disease and erythromelalgia. The symptoms came on in attacks, and had so far recurred three times.

The third case was one seen in Dr. Dana's clinic some years ago. The patient was a boy of fourteen, with a profoundly neuropathic family history, who had had about half a dozen attacks of periodic paralysis. At the time Dr. Dana suggested that malaria might be at the bottom of his trouble. Some of the clinical aspects of the case simulated a low grade of poliomyelitis, but it was subsequently decided that the apparent atrophy of the muscles was the result of emaciation. The vasomotor symptoms predominated, and no sensory disturbances were present.

Dr. Taylor, in closing, said he thought the cases which had been mentioned by the various speakers were not absolutely analogous to those reported in his paper. In reply to a question, the speaker said that the sphincters in his case were not affected. In some of the cases the muscles of respiration were involved; in others not. In one case there was dangerous dyspnœa. No sensory changes could be found. The clinical aspects of the condition were so absolutely unique and characteristic that an error in diagnosis was hardly possible, viz., periodic paralysis of the muscles of the trunk and extremities, associated with loss of reflex and electrical excitability during the attack, and occurring as a family affection, with normal conditions between. The cases cited by the various speakers evidently did not belong to this type, although possibly, they were related. Hysteria was evidently not to be considered, and malaria had no constant place in the etiology, nor was there sufficient evidence to show that the vasomotor system played any prominent part in its production. A temporary autointoxication seemed the most probable cause, the nature of which remains wholly unknown.

226. REMARKS ON SPINAL IRRITATION. Hugh T. Patrick, M.D., (Medicine, 3, 1897, p. 535).

The term "spinal irritation" should be banished from medical nomenclature. The pain and tenderness along the spine commonly known by this name have nothing to do with the spinal cord or its membranes, or with the spinal column. The condition is not due to congestion of anæmia of the cord, or altered nutrition, or a neurosis of the spinal arteries, or thickening of the membranes, or exhaustion of the gray matter of the cord, or an affection of the nerve roots or trunks, or irritation of vertebræ or spinal ganglia, or any other permanent condition in the back whatsoever. In so-called spinal irritation there are tender points along the spine. It can, however, be shown that these points shift rapidly, absolutely changing their position within five or ten minutes. The sore points are notoriously inconstant in degree of tenderness and in location, but it seems to be not generally known that the patient can locate them only about as accurately as a well person can locate a spot on his back previously touched. The tenderness cannot be due to anything abnormal at the tender spot, else the pressure the second time on the same spot would be just as painful as the first time, and, furthermore, we cannot suppose a pathological condition to have developed within five or ten minutes. This shifting corresponds just about to that in the healthy individual. If a normal person have any given spot on the back pressed, after five or ten minutes he will be unable to indicate exactly where the spot is. It seems reasonable to conclude that there is a lack of absolute accuracy of the sensorium. In the pathological case the shifting involves the sudden disappearance of pain from one place and its appearance in another. The inference is that the pain or pressure is itself due to the perverted mechanism of sensory reception and registration in the brain, or to a perverted reaction of still higher centres, constituting a vicious consciousness. A proclaimed diagnosis of spinal iritation may have an exceedingly bad effect upon a nervous patient. The presence of tenderness of the back with shifting sensitive spots, although indicating a functional nervous affection located entirely in the cerebrum, does not in any way preclude the presence, in addition, of organic disease of the brain, cord, or any other viscus. The almost instantaneous disappearance of tenderness from one point and its simultaneous appearance at another is not of itself proof of simulation, malingering, or nervous nonsense on the part of the patient. FREEMAN.